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(54) Title: GLYPICANS FOR THE DETECTION AND TREATMENT OF HUMAN CARCINOMA

(57) Abstract

Glycosylphosphatidylinositol- (GPI-) anchored HSPG glypican-1 is strongly expressed in human breast and pancreatic cancer - both by the cancer cells and in the case of pancreatic cancer the adjacent fibroblasts - whereas expression of glypican-1 is low in the normal pancreas and in chronic pancreatitis. Treatment of two pancreatic cancer cell lines, which express glypican-1, with the enzyme phosphoinositide-specific phospholipase-C (PI-PLC) abrogated their mitogenic responses to two heparin-binding growth factors: fibroblast growth factor-2 (FGF2) and heparin-binding EGF-like growth factor (HB-EGF). Treatment of MDA-MB-231 and MDA-MB-468 breast cancer cells with PI-PLC abrogates the mitogenic response to two heparin-binding growth factors, heparin-binding epidermal growth factor-like growth factor (HB-EGF) and fibroblast growth factor-2 (FGF-2). Syndecan-1 is also expressed at high levels in breast cancer tissues as well as breast cancer cells by comparison with breast normal tissues. Temporary or permanent transfection of a glypican-1 antisense construct attenuated glypican-1 protein levels and the mitogenic response to FGF2 and HB-EFG. Glypican can be used to detect the carcinoma *in vitro* and therapeutics that either bind to (*e.g.*, antibodies or drugs), remove (*e.g.*, enzymes) or prevent the expression (*e.g.*, antisense constructs) of surface of the extracellular domain of glypican-1 are effective in retarding the growth of glypican-responsive carcinomas.

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